57, 64, 66, and 72. The proposed amendments are made without prejudice or disclaimer. Reconsideration of the application as proposed to be amended herein is respectfully requested.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1, 4, 5, 16, 17, 57, 64, and 72 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 4, 5, 16, 17, 57, 64, and 72 have each been amended. It is respectfully submitted that each of these claims, as amended, is in condition for allowance. Accordingly, it is respectfully requested that the 35 U.S.C. § 112, first paragraph, rejection of these claims be withdrawn.

Rejections Under 35 U.S.C. § 103(a)

Miura in View of Wang and Further in View of Northrup and Turner

Claims 1, 3, 4, 12-25, 29, 30-34, 38-44, 50-64, 73-74, and 105-107 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent 5,132,012 to Miura et al. (hereinafter "Miura") in view of U.S. Patent 5,663,488 to Wang et al. (hereinafter "Wang"), and further in view of U.S. Patent 5,882,496 to Northrup et al. (hereinafter "Northrup") and U.S. Patent 5,885,869 to Turner et al. (hereinafter "Turner"). Applicant respectfully traverses this rejection, as hereinafter set forth.

M.P.E.P. 706.02(j) sets forth the standard for a Section 103(a) rejection:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings. Second, there must be a reasonable expectation of success. Finally, **the prior art reference (or references when combined) must teach or suggest all the claim limitations.** The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on

applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). (Emphasis added).

Miura discloses a liquid chromatograph including a silicon or borosilicate glass substrate with an elongate channel, or conduit, formed therein. The liquid chromatograph of Miura also includes a field effect transistor-type chemical sensor associated with the channel. The component ions of a sample are detected by the chemical sensor as they flow through the channel, past the chemical sensor. Miura does not disclose the use of a matrix of porous silicon as the channel.

Wang teaches an analytical instrument, such as a gas chromatograph, that includes a thermal isolation system with a pumping assembly operatively and a closed cavity operatively associated with the pumping assembly. The pumping assembly changes the pressure in the closed cavity so as to provide selective control over the extent of thermal isolation therein while reducing the operation of a thermal device to control the extent of thermal isolation in the closed cavity. Thus, the pumping assembly provides control in the extend of thermal isolation in the closed cavity while reducing the amount of power consumed by the thermal device. The analytical instrument also includes a component system, such as a gas chromatograph separation column, located within the closed cavity. Changes in the extent of thermal isolation in the closed cavity effect separations in a gas chromatography column. The use of pressure to effect changes in the extent of thermal isolation also decreases the time in which such changes can be effected, thereby increasing the number of separations that can be made during a certain period of time. Wang also discloses that miniaturized chromatographic devices, including those fabricated on silicon substrates, can be used with the thermal isolation system. Wang does not, however, disclose the use of a chromatograph that includes a porous silicon separation column.

Northrop discloses porous silicon structures for use in filtering and valving devices. While it is acknowledged that Northrop, in the Abstract, discloses "[f]abrication and use of porous silicon structures to increase surface area of . . . electrophoresis devices . . .", this disclosure of the use of porous silicon in Northrop is limited to applications in chemical or biological filters that prevent molecules of certain sizes from flowing therethrough, thermally

controlled valves, and valves that control the flow of electrically charged chemicals therethrough.

The thermally controlled valves disclosed in Northrop include a heating element adjacent the porous silicon. Upon heating the porous silicon, a sample is forced therethrough. Northrop, in FIGs. 4 and 5 and at col. 6, lines 5-37, provides an example wherein the thermally controlled valve controls the flow of a sample from a polymerase chain reaction ("PCR") apparatus to an electrophoresis channel. The electrophoresis channel is formed as a groove or microchannel, and does not include a matrix of porous silicon.

Northrop discloses that, due to the precision with which pores of a desired size can be formed in porous silicon, the porous silicon is useful for filtering chemical or biological samples and removing molecules that are larger than the pores therefrom.

Northrop provides that the flow of electrically charged chemicals through the pores can be controlled in the same manner as electrophoresis is effected; that is, the flow of electrically charged chemicals through the pores can be effected by creating a potential difference across the porous silicon structure. Northrop does not disclose that porous silicon is actually useful for providing a matrix in a sample separation column.

Turner teaches a method of forming uniformly doped hemispherical gain polycrystalline silicon. Turner does not contemplate separating the constituents of a sample in a chromatograph, electrophoretic apparatus, or other separation device.

Lack of Motivation to Combine

It is respectfully submitted that neither the cited references themselves nor the knowledge generally available to one of ordinary skill in the art provide any motivation to one of ordinary skill to combine the references in the manner suggested in the outstanding Office Action. Specifically, one of ordinary skill would not have been motivated to combine the teachings of Miura, Wang, Northrop, and Turner to develop a device with a substrate and a porous matrix extending a distance across the substrate.

As indicated previously herein, the Patent Office bears the burden of establishing a *prima facie* case of obviousness. This burden can only be satisfied

> by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art *would lead* that individual to combine the relevant teachings of the references. In re Fine, 837 F.2d 1071, 1074, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988). Indeed, the teachings of references can be combined only if there is some suggestion or incentive to do so. ACS Hospital Systems, Inc. v. Montefiore Hospital, 723 F.2d 1572,1577, 221 U.S.P.Q. 929, 933 (Fed. Cir. 1984).

Ex parte Obukowicz, 27 USPQ2d 1063 (B.O.P.A.I. 1993).

While Miura teaches a spiral capillary column that may be formed in a silicon wafer, Miura does not suggest a further need for shortening the length of the column by use of a porous matrix or otherwise. Wang merely mentions that miniaturized silicon chromatographs could be used in the thermal isolation system disclosed therein. Wang does not suggest that it would be useful to shorten the length of the chromatograph by use of a porous matrix or otherwise. Northrop mentions electrophoretic separation apparatus, but only to describe the manner in which the flow of electrically charged chemicals through a porous silicon valve could be controlled and to disclose the use of a thermally activated porous silicon valve for introducing a sample into an electrophoresis apparatus. Finally, Turner neither mentions separation apparatus nor suggests that hemispherical grain silicon or roughened silicon would be useful in the columns thereof. Nor has any motivation to combine been provided from the knowledge generally available to those of ordinary skill in the art.

Based on the lack of motivation in the references and the art, it appears that the combination of Miura, Wang, Northrop, and Turner could only have been based on hindsight provided by the disclosure of the referenced patent application. *See, e.g., In re Fritch*, 23 USPQ2d 1780 (Fed. Cir. 1992); *In re Fine*, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988).

Therefore, it is respectfully submitted that these references would not have motivated one of skill in the art to make the proposed combination. Accordingly, it is respectfully submitted that each of claims 1, 3, 4, 12-25, 29, 30-34, 38-44, 50-64, 73-74, and 105-107 is allowable under 35 U.S.C. § 103(a).

Failure to Teach All of the Claim Limitations

In addition, it is respectfully submitted that Miura, Wang, Northrop, and Turner, taken alone or in any combination, do not teach or suggest every element of the claims, as proposed to be amended herein.

Independent claim 1, as proposed to be amended herein, recites a sample separation apparatus that includes a semiconductor substrate comprising at least one of silicon, gallium arsenide, and indium phosphide with a matrix with a first porous region extending a distance across the substrate.

It is respectfully submitted that none of Miura, Wang, Northrop, or Turner, taken alone or in combination, teaches or suggests a sample separation apparatus with each of the elements recited in claim 1, as proposed to be amended. While Miura and Northrop disclose sample separation apparatus that may include a silicon substrate with a channel or groove recessed therein, neither of these references teaches or suggests a matrix with a first porous region extending a distance across the silicon substrate. Northrop teaches the use of porous silicon structures in filters, thermally controllable valves, and electrically controllable valves, but does not teach or suggest apparatus that include a matrix comprising a first porous region extending a distance across a substrate including at least one of silicon, gallium arsenide, and indium phosphide. Finally, Turner does not teach or suggest a matrix with a first porous region extending a distance across a substrate including at least one of silicon, gallium arsenide, and indium phosphide.

Accordingly, it is respectfully submitted that claim 1, as proposed to be amended herein, is allowable over the combination of Miura, Wang, Northrop, and Turner.

Claims 3, 4, 12-25, and 29 are each allowable as depending either directly or indirectly from claim 1, which is allowable.

Claim 16 is further allowable since none of Miura, Wang, Northrop, or Turner teaches or suggests a processor on the substrate. Rather, the processor of Miura is separate from the substrate, as depicted in FIG. 9 thereof.

Claim 17 is further allowable since none of Miura, Wang, Northrop, or Turner teaches or suggests a memory device on the substrate. It is believed that Miura does not even teach or suggest associating a memory device with the liquid chromatograph disclosed therein.

Independent claim 30, as proposed to be amended herein, recites a separation apparatus that includes a substrate of a material, at least one capillary column formed in the substrate of the material, and a detector situated adjacent the capillary column. Claim 30, as proposed to be amended, also recites that the capillary column comprises a first porous matrix.

It is respectfully submitted that none of Miura, Wang, Northrop, or Turner, taken alone or in combination, teaches or suggests a capillary column formed in a material of a substrate and comprising a porous matrix. Accordingly, it is respectfully submitted that claim 30, as proposed to be amended, is allowable over the combination of Miura, Wang, Northrop, and Turner.

Claims 31-34, 38-44, and 50 are each allowable as depending either directly or indirectly from claim 30, which is allowable.

Claim 43 is further allowable since none of Miura, Wang, Northrop, or Turner teaches or suggests a processor on the substrate. Rather, the processor of Miura is separate from the substrate, as depicted in FIG. 9 thereof.

Claim 44 is further allowable since none of Miura, Wang, Northrop, or Turner teaches or suggests a memory device on the substrate. It is believed that Miura does not even teach or suggest associating a memory device with the liquid chromatograph disclosed therein.

Independent claim 51, as proposed to be amended herein, recites a miniature chromatograph that includes a substrate of a material and a porous matrix formed in the material of the substrate. The porous matrix comprises at least one capillary column.

It is respectfully submitted that none of Miura, Wang, Northrop, and Turner, taken alone or in combination, teaches or suggests every element of claim 51, as proposed to be amended. While Miura and Wang teach, among other things, miniature chromatographs that include capillary columns, neither of these references teaches or suggests a porous matrix that comprises the capillary column. Moreover, Northrop, teaches porous silicon matrices, but does not teach or suggest a porous matrix comprising at least one capillary column of a miniature chromatograph

that is formed in a material of the substrat thereof. Turner includes n teaching or suggestion of a porous matrix or of a capillary column.

Accordingly, it is respectfully submitted that claim 51, as proposed to be amended, is allowable over the combination of Miura, Wang, Northrop, and Turner.

Claims 52-56 are each allowable as depending either directly or indirectly from claim 51, which is allowable.

Independent claim 57, as proposed to be amended herein, recites an electrophoretic apparatus that includes a substrate, at least one sample column in the substrate, and a control column in the substrate. The at least one sample column comprises a first porous matrix. The control column comprises a second porous matrix.

It is respectfully submitted that the combination of Miura, Wang, Northrop, and Turner does not teach or suggest every element of claim 57, as proposed to be amended. Specifically, none of these references teaches or suggests a control column. Moreover, none of these references teaches or suggests a column that includes a porous matrix.

Accordingly, it is respectfully submitted that claim 57, as proposed to be amended, is allowable over the combination of Miura, Wang, Northrop, and Turner.

Claims 58-63 are each allowable as depending either directly or indirectly from claim 57, which is allowable.

Independent claim 64, as proposed to be amended herein, recites an analyte detection apparatus that includes a substrate and a matrix formed in the material of the substrate. The substrate comprises silicon. The matrix comprises at least one porous silicon column.

It is respectfully submitted that the combination of Miura, Wang, Northrop, and Turner does not teach or suggest every element recited in claim 64, as proposed to be amended. Specifically, none of these references teaches or suggests a matrix that comprises at least one porous silicon column.

Claims 73 and 74 are each allowable as depending from claim 64, which is allowable.

Independent claim 105 recites an ultrasmall flow channel device that includes a fluid inlet and a flow channel connected to the fluid inlet. The flow channel includes a matrix of hemispherical grain silicon.

It is respectfully submitted that the combination of Miura, Wang, Northrop, and Turner does not teach or suggest a flow channel including a matrix of hemispherical grain silicon. By way of contrast, Miura, Wang, and Northrop teach open flow channels. Turner does not teach a flow channel at all. Rather, Turner merely teaches methods of uniformly doping hemispherical grain silicon and roughened silicon layer independently of other layer of a semiconductor substrate.

Accordingly, it is respectfully submitted that claim 105 is allowable over Miura, Wang, Northrop, and Turner, taken alone or in any combination.

Claims 106 and 107 are each allowable as depending either directly or indirectly from claim 105, which is allowable.

For these reasons, it is respectfully requested that the rejection of claims 1, 3-4, 12-25, 29, 30-34, 38-44, 50-65, 73-74, and 105-107 as being rendered obvious by the combination of Miura, Wang, Northrop, and Turner be withdrawn.

Miura in View of Swedberg and Sunzeri, and Further in View of Northrup and Turner

Claims 1, 3-12, 14-17, 25-38, 42-52, 54-64, 66-69, 71-74, and 105-107 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Miura in view of U.S. Patent 5,571,410 to Swedberg et al. (hereinafter "Swedberg") and U.S. Patent 5,536,382 to Sunzeri (hereinafter "Sunzeri"), and further in view of Northrup and Turner.

The subject matter disclosed in Miura, Wang, Northrop, and Turner has been summarized previously herein.

Swedberg discloses a miniaturized separation apparatus including a column within which a porous quantity of biocompatible material, such as "nylon, cellulose, polymethylmethacrylate, polyacrylamide, agarose, or the like" may be disposed. Col. 27, lines 37-40. Swedberg does not

teach that the porous matrix is formed in the substrate. Rather, a quantity of biocompatible, porous material is placed into an open column.

Sunzeri teaches a method for analyzing the constituents of human biological fluids. The human biological fluids are separated by way of known capillary electrophoresis techniques and compared to a control, which provides a standard for quantitation.

Lack of Motivation to Combine

The lack of a motivation to one of ordinary skill to combine the teachings of Miura, Wang, Northrop, and Turner to come up with the subject matter recited in the claims of the reference application was discussed previously herein.

It is further submitted that neither Swedberg nor Sunzeri provides the missing motivation to combine the references in the manner that has been suggested in the outstanding Office Action.

In particular, while Swedberg discloses that a quantity of biocompatible, porous material, such as nylon, cellulose, polymethylmethacrylate, polyacrylamide, or agarose, may be disposed into an open capillary column, Swedberg does not provide one of skill in the art with any motivation to form a porous matrix in a substrate that includes silicon, gallium arsenide, or indium phosphide, as recited in the pending claims. It is well known that all of the biocompatible materials listed in Swedberg are useful for electrophoretically separating samples. The use of a porous matrix formed in a substrate is not presently known, however. Accordingly, it is respectfully submitted that Swedberg does not provide the motivation missing from Miura, Wang, Northrop, and Turner.

Moreover, Sunzeri merely discloses a method for separating the constituents of a human biological sample using capillary electrophoretic techniques. In that method, the sample is compared to a control. While Sunzeri discloses the use of fused silica (i.e., sand) capillaries, it includes no teaching or suggestion of the use of an apparatus including a substrate and a porous matrix formed in the substrate. Accordingly, Sunzeri also fails to provide the motivation lacking from Miura, Wang, Northrop, Turner, and Swedberg.

Accordingly, it is respectfully submitted that, based on the teachings of the cited references and the knowledge generally available to one of ordinary skill in the art, one of ordinary skill would not be motivated to combine the teachings of Miura, Wang, Northrop, Turner, Swedberg, and Sunzeri in the manner that has been suggested in the outstanding Office Action to render the pending claims obvious.

Moreover, as neither the references themselves nor the generally available knowledge in the art provide such motivation, it appears that the combination of Miura, Wang, Northrop, Turner, Swedberg, and Sunzeri is based on the disclosure provided by the referenced patent application and, therefore, constitutes impermissible hindsight.

For these reasons, it is respectfully requested that the section 103(a) rejection of claims 1, 3-12, 14-17, 25-38, 42-52, 54-64, 66-69, 71-74, and 105-107 as being rendered obvious by the combination of Miura, Wang, Northrop, Turner, Swedberg, and Sunzeri be withdrawn.

Failure to Teach All of the Claim Limitations

In addition, it is respectfully submitted that Miura, Wang, Northrop, Turner, Swedberg, and Sunzeri, taken alone or in any combination, do not teach or suggest every element of the claims, as proposed to be amended herein.

It is respectfully submitted that the combination of Miura, Wang, Northrop, Turner, Swedberg, and Sunzeri does not teach or suggest a sample separation apparatus with each of the elements recited in claim 1, as proposed to be amended. While Miura and Northrop disclose sample separation apparatus that may include a silicon substrate with a channel or groove recessed therein, neither of these references teaches or suggests a matrix with a first porous region extending a distance across the silicon substrate. Northrop teaches the use of porous silicon structures in filters, thermally controllable valves, and electrically controllable valves, but does not teach or suggest apparatus that include a matrix comprising a first porous region extending a distance across a substrate including at least one of silicon, gallium arsenide, and indium phosphide. Turner does not teach or suggest a matrix with a first porous region extending a distance across a substrate including at least one of silicon, gallium arsenide, and

indium phosphide. Swedberg teaches use of a porous matrix in the column thereof, but the porous matrix is a conventional separation matrix material, such as "nylon, cellulose, polymethylmethacrylate, polyacrylamide, agarose, or the like" placed into an open channel or groove. Swedberg neither teaches nor suggests that the porous matrix is "formed of [the] material of [the] substrate". Finally, Sunzeri does not teach or suggest the use of a sample separation apparatus with "a substrate comprising at least one of silicon, gallium arsenide, and indium phosphide" or "a matrix formed of [the] material of [the] substrate . . . [and] comprising a first porous region extending a distance across [the] substrate."

Accordingly, it is respectfully submitted that claim 1, as proposed to be amended herein, is allowable over the combination of Miura, Wang, Northrop, Turner, Swedberg, and Sunzeri.

Claims 3-12, 14-17, and 25-29 are each allowable as depending either directly or indirectly from claim 1, which is allowable.

Claim 5 is further allowable since none of Miura, Wang, Northrop, Turner, Swedberg, or Sunzeri teaches or suggests a "second porous region extending a distance across said substrate." By way of contrast, Sunzeri merely discloses the use of a control, it does not teach or suggest an apparatus with a second porous region extending a distance across a substrate comprising at least one of silicon, gallium arsenide, and indium phosphide.

Claim 6, which depends from claim 5, is also allowable since none of Miura, Wang, Northrop, Turner, Swedberg, or Sunzeri teaches or suggests a "second porous region [that] comprises a control column."

Claim 7 is further allowable since none of Miura, Wang, Northrop, Turner, Swedberg, or Sunzeri teaches or suggests "a reaction region immediately situated along the length of an continuous with [the] first porous region" of the sample separation apparatus.

Claim 8, which depends from claim 7, is further allowable because none of Miura, Wang, Northrop, Turner, Swedberg, or Sunzeri teaches or suggests a reaction region that comprises a capture component.

Claim 9, which depends from claim 7, is further allowable since none of Miura, Wang, Northrop, Turner, Swedberg, or Sunzeri teaches or suggests a sample separation apparatus with a

reaction region situated a predetermined distance from an end of a first porous region of the sample separation apparatus.

Claim 10, which depends from claim 5, is further allowable because none of Miura, Wang, Northrop, Turner, Swedberg, or Sunzeri teaches or suggests a sample separation apparatus that includes two porous regions, each including a region situated immediately along the length thereof.

Claim 11 depends from claim 10, and is further allowable since none of Miura, Wang, Northrop, Turner, Swedberg, or Sunzeri teaches or suggests that the distances between the reaction regions and the ends of the corresponding porous regions are substantially the same.

Claim 16 is further allowable since none of Miura, Wang, Northrop, Turner, Swedberg, or Sunzeri teaches or suggests a processor on the substrate. Rather, the processor of Miura is separate from the substrate, as depicted in FIG. 9 thereof.

Claim 17 is further allowable since none of Miura, Wang, Northrop, Turner, Swedberg, or Sunzeri teaches or suggests a memory device on the substrate. It is believed that Miura does not even teach or suggest associating a memory device with the liquid chromatograph disclosed therein.

Independent claim 30, as proposed to be amended herein, recites a separation apparatus that includes a substrate, at least one capillary column formed in the substrate, and a detector situated adjacent the capillary column. Claim 30, as proposed to be amended, also recites that the capillary column comprises a first porous matrix formed in the material of the substrate.

It is respectfully submitted that none of Miura, Wang, Northrop, Turner, Swedberg, and Sunzeri, taken alone or in combination, teaches or suggests a capillary column formed in a substrate of a material and comprising a porous matrix formed in the substrate. Accordingly, it is respectfully submitted that claim 30, as proposed to be amended, is allowable over the combination of Miura, Wang, Northrop, Turner, Swedberg, and Sunzeri.

Claims 31-38 and 42-50 are each allowable as depending either directly or indirectly from claim 30, which is allowable.

Claim 43 is further allowable since none of Miura, Wang, Northrop, Turner, Swedberg, or Sunzeri teaches or suggests a processor on the substrate. Rather, the processor of Miura is separate from the substrate, as depicted in FIG. 9 thereof.

Claim 44 is further allowable since none of Miura, Wang, Northrop, Turner, Swedberg, or Sunzeri teaches or suggests a memory device on the substrate. It is believed that Miura does not even teach or suggest associating a memory device with the liquid chromatograph disclosed therein.

Claim 45 is further allowable since none of Miuta, Wang, Northrop, Turner, Swedberg, or Sunzeri teaches or suggests a separation apparatus with at least capillary columns formed in the substrate thereof. By way of contrast with claim 45, Sunzeri merely teaches the testing of a control, or standard, for purposes of comparison, not a separation apparatus with at least one capillary column comprising a porous matrix formed in the material of the substrate and at least another capillary column formed in the substrate.

Claim 46, which depends from claim 45, is further allowable because none of Miura, Wang, Northrop, Turner, Swedberg, or Sunzeri teaches or suggests that the two or more capillary columns each have substantially equal lengths.

Claim 47, which depends from claim 45, is further allowable because none of Miura, Wang, Northrop, Turner, Swedberg, or Sunzeri teaches or suggests that the "at least another capillary column comprises a second porous matrix."

Claim 48, which depends from claim 47, is further allowable since none of Miura, Wang, Northrop, Turner, Swedberg, or Sunzeri teaches or suggests a separation apparatus with at least two columns comprising porous matrices, the at least two columns comprising substantially equal surface areas.

Claim 49, which depends from claim 48, is also allowable because none of Miura, Wang, Northrop, Turner, Swedberg, or Sunzeri teaches or suggests that the at least two columns comprise substantially equal volumes.

Independent claim 51, as proposed to be amended herein, recites a miniature chromatograph that includes a substrate and a porous matrix formed in the material of the substrate. The porous matrix comprises at least one capillary column.

It is respectfully submitted that none of Miura, Wang, Northrop, Turner, Swedberg, and Sunzeri, taken alone or in combination, teaches or suggests every element of claim 51, as proposed to be amended. While Miura and Wang teach, among other things, miniature chromatographs that include capillary columns, neither of these references teaches or suggests a porous matrix that comprises the capillary column. Moreover, Northrop, teaches porous silicon matrices, but does not teach or suggest a porous matrix formed in the material of a substrate of a miniature chromatograph and comprising at least one capillary column of the miniature chromatograph. Turner includes no teaching or suggestion of a porous matrix or of a capillary column. Swedberg discloses a miniature separation apparatus that may include columns with a porous matrix, but does not teach or suggest a porous matrix that is formed in the material of the substrate thereof. Sunzeri only discloses the use of known capillary electrophoresis devices. Sunzeri does not teach or suggest a miniature chromatograph that includes a substrate and a porous matrix formed in and integral with the substrate or that the porous matrix comprises at least one capillary column.

Accordingly, it is respectfully submitted that claim 51, as proposed to be amended, is allowable over the combination of Miura, Wang, Northrop, Turner, Swedberg, and Sunzeri.

Claims 52 and 54-56 are each allowable as depending either directly or indirectly from claim 51, which is allowable.

Independent claim 57, as proposed to be amended herein, recites an electrophoretic apparatus that includes a substrate, at least one sample column formed in the material of the substrate, and a control column in the substrate. The at least one sample column comprises a first porous matrix. The control column comprises a second porous matrix formed in the material of the substrate.

It is respectfully submitted that the combination of Miura, Wang, Northrop, Turner, Swedberg, and Sunzeri does not teach or suggest every element of claim 57, as proposed to be

amended. While Sunzeri teaches use of a control, Sunzeri does not teach or suggest the use of an apparatus with a substrate, at least one sample column formed in the material of the substrate, and a control column that includes pores that are formed in the material of the substrate.

Accordingly, it is respectfully submitted that claim 57, as proposed to be amended, is allowable over the combination of Miura, Wang, Northrop, and Turner.

Claims 58-63 are each allowable as depending either directly or indirectly from claim 57, which is allowable.

Independent claim 64, as proposed to be amended herein, recites an analyte detection apparatus that includes a substrate of silicon and a matrix formed in the silicon. The substrate comprises silicon. The matrix comprises at least one porous silicon column.

It is respectfully submitted that the combination of Miura, Wang, Northrop, Turner, Swedberg, and Sunzeri does not teach or suggest every element recited in claim 64, as proposed to be amended. Specifically, none of these references teaches or suggests a matrix comprising at least one porous silicon column, the matrix being formed in a substrate comprising silicon.

Claims 66-69 and 71-74 are each allowable as depending from claim 64, which is allowable.

Claim 71 is also allowable since none of Miura, Wang, Northrop, Turner, Swedberg, or Sunzeri teaches or suggests a reaction region along the length of the porous column.

Claim 72 is further allowable since none of Miura, Wang, Northrop, Turner, Swedberg, or Sunzeri teaches or suggests a control column on the substrate.

Independent claim 105 recites an ultrasmall flow channel device that includes a fluid inlet and a flow channel connected to the fluid inlet. The flow channel includes a matrix of hemispherical grain silicon.

It is respectfully submitted that the combination of Miura, Wang, Northrop, Turner, Swedberg, and Sunzeri does not teach or suggest a flow channel including a matrix of hemispherical grain silicon. By way of contrast, Miura, Wang, and Northrop, teach open flow channels. Swedberg only teaches or suggests a channel that is fill with a convention, porous separation material, such as "nylon, cellulose, polymethylmethacrylate, polyacrylamide, agarose,

or the like", not a flow channel including a matrix of hemispherical grain silicon. Sunzeri only teaches of suggests the use of known apparatus, such as capillary electrophoresis apparatus. Turner does not teach a flow channel at all. Rather, Turner merely teaches methods of uniformly doping hemispherical grain silicon and roughened silicon layer independently of other layer of a semiconductor substrate.

Accordingly, it is respectfully submitted that claim 105 is allowable over Miura, Wang, Northrop, Turner, Swedberg, and Sunzeri, taken alone or in any combination.

Claims 106 and 107 are each allowable as depending either directly or indirectly from claim 105, which is allowable.

For these reasons, it is respectfully requested that the rejection of claims 1, 3-12, 14-17, 25-38, 42-52, 54-64, 66-69, 71-74, and 105-107 as being rendered obvious by the combination of Miura, Wang, Northrop, and Turner be withdrawn.

Claim 70

Claim 70, which depends from claims 69, 66, 65, and 64, was not specifically rejected in the outstanding Office Action. Claim 70 has not been withdrawn from consideration or canceled. In the Office Action dated July 21, 1999 under 35 U.S.C. § 112, second paragraph, claim 70 was only rejected "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." This rejection has been overcome. Accordingly, it is respectfully submitted that claim 70 is allowable.

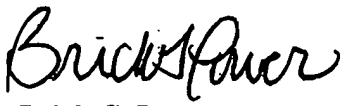
ENTRY OF AMENDMENTS

The amendments proposed above should be entered because the amendments are supported by the as-filed specification and drawings and do not add any new matter to the application. Further, the amendments do not raise new issues or require a further search. Finally, if it is determined that the amendments do not place the application in condition for allowance, entry is respectfully requested upon filing of a Notice of Appeal herein.

CONCLUSION

Claims 1, 3-64, 66-74, and 105-107 are believed to be in condition for allowance, and an early notice thereof is respectfully solicited. Should additional issues remain which might be resolved by a telephone conference, the Office is respectfully invited to contact Applicant's undersigned attorney.

Respectfully Submitted,



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